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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,583	05/03/2002	Dan L. Eaton	10466/350	2698

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EXAMINER	
HUNNICUTT, RACHEL KAPUST	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,583	EATON ET AL.	
	Examiner	Art Unit	
	Rachel K. Hunnicutt	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1104*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

Applicant's amendment filed November 5, 2004 is acknowledged. Claims 1-10 have been amended. Claims 1-13 are pending and under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The objection to the specification regarding the use of trademarks is withdrawn in response to Applicant's amendments to the specification.

The rejection of claims 1-6 and 10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, is withdrawn in response to Applicants' amendments to the claims.

The rejection of claims 1-11 under 35 U.S.C. 102(a) as being anticipated by Fujikawa-Adachi et al. is withdrawn. The declaration filed on November 5, 2004 under 37 CFR 1.131 is sufficient to overcome the Fujikawa-Adachi et al. reference.

The rejection of claims 12 and 13 under 35 U.S.C. 103(a) as being unpatenable over Fujikawa-Adachi et al. in view of U.S. Patent No. 5,639,597 is withdrawn in response to Applicants' arguments on p. 20 of the response.

Claim Objections/Rejections Maintained

Claim Rejections - 35 USC § 101

The rejection of claims 1-13 under 35 U.S.C. 101 is maintained for reasons of record on p. 3-4 of the office action of paper no. 0704.

Applicants argue that the PRO1335 polypeptide is differentially expressed in certain cancers compared to normal tissue and is useful as a diagnostic tool. Applicants refer to

Example 18 which shows that the gene encoding PRO1335 is more highly expressed in normal stomach, lung, rectal, and skin tissue compared to stomach, lung, rectal, and melanoma tumor tissue, respectively. The Exhibit 1 declaration of J. Christopher Grimaldi teaches that the DNA libraries used in the gene expression studies were made from pooled samples of normal and of tumor tissues. Grimaldi states in section 6 that "I conducted a semi-quantitative analysis of the expression of the DNA sequences of interest in normal versus tumor tissues. Expression levels were graded according to a scale of +, -, and +/- to indicate the amount of the specific signal detected. Using the widely accepted technique of PCR, it was determined whether the polynucleotides tested were more highly expressed, less expressed, or whether expression remained the same in tumor tissue as compared to its normal counterpart. Because this technique relies on the visual detection of ethidium bromide staining of PCR products on agarose gels, it is reasonable to assume that any detectable differences seen between two samples will represent at least a two fold difference in cDNA."

Furthermore, in Exhibit 2, another declaration of J. Christopher Grimaldi, Grimaldi states that when a gene is overexpressed, the gene product or polypeptide will also be overexpressed (p. 13 of response). The declaration of Dr. Paul Polakis avers that mRNA levels typically correlate with an increase in abundance of the encoded protein (p. 13 of response). Applicants further cite Orntoft *et al.*, Hyman *et al.*, and Pollack *et al.* in support of the argument that in the vast majority of cases, the combined teachings of the art teach that gene amplification influences gene expression and that gene expression influences protein levels. In addition, Applicants refer to the declaration of Dr. Ashkenazi and cited references Hanna and Mornin who teach that even if higher levels of mRNA do not correlate with an increase in abundance of the encoded protein, that type of information is also useful in diagnosing and treating patients.

Applicants' arguments have been fully considered but have not been found to be persuasive. A utility of being a diagnostic target for stomach, lung, rectal, and melanoma tumors is a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use. This is not a substantial utility. In Example 18, the specification merely states that the gene is "more highly expressed" in one tissue as compared to another. There is no guidance in the specification as to how high the levels are. The declaration of Grimaldi (Exhibit 1) does not teach the level of reproducibility or the level of reliability of the

results. Neither the specification nor the declarations provide any evidence that indicates what the differences were or whether the results were statistically significant. Applicants have provided no indication of the nature or number of samples that were used. In addition, one cannot determine from the data in the specification whether the observed "amplification" of nucleic acid is due to increase in chromosomal copy number, or alternatively due to an increase in transcription rates. The only thing Applicants teach is that the gene was "more highly expressed", and this does not enable the skilled artisan to differentiate amongst expression levels in order to diagnose any diseases.

At paragraph 4 of the second Grimaldi declaration (Exhibit 2), the declarant discusses mutations of Her2/Neu, and chromosomal translocations that are known to be associated with cancer, and states that "If the chromosomal aberration results in the aberrant expression of a mRNA and the corresponding gene product (the polypeptide) as they do in the aforementioned cases, then the gene product is a promising target for cancer therapy, for example, by the therapeutic antibody approach." This argument has been fully considered but is not deemed persuasive because it evinces that the instant specification provides a mere invitation to experiment, and not a readily available utility. The PRO1335 gene, unlike Her2/Neu, has *not* been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. Similarly, unlike t(5;14), no translocation of PRO1335 is known to occur. All that the specification demonstrates is that the PRO1335 nucleic acid was more highly expressed in normal stomach, lung, rectal, and skin tissue compared to stomach, lung, rectal, and melanoma tumor tissue. No mutation or translocation of PRO1335 has been associated with stomach cancer, lung cancer, rectal cancer, or melanomas. In the absence of any of the above information, all that the specification does is present evidence that the DNA encoding PRO1335 is amplified in an unknown number of samples, and invite the artisan to determine the rest of the story. Such is insufficient to meet the requirements of 35 U.S.C. §101 for the claimed protein.

Whether or not increased levels of PRO1335 mRNA correlate with increased levels of PRO1335 protein is not an issue. The declarations and cited references do not establish a substantial utility for the PRO1335 nucleic acid molecules. As stated above, the specification does not provide sufficient guidance to the skilled artisan to diagnose or treat any disease. Thus,

the claimed protein encoded by PRO1335 does not have a specific and substantial or well-asserted utility.

Claim Rejections - 35 USC § 112

The rejection of claims 1-13 under 35 U.S.C. 112, first paragraph, for lack of enablement due to the invention not being supported by a specific or substantial asserted utility or a well-established utility, is maintained for reasons of record on p. 5 of paper no. 0704.

The rejection of claims 1-5 and 12-13 under 35 U.S.C. 112, first paragraph, for lack of enablement, is maintained for reasons of record on p. 5-6 of paper no. 0704.

Applicants argue that the claims have been amended to recite the functional limitation "wherein said isolated polypeptide is more highly expressed in normal stomach, lung, rectal or skin tissue compared to stomach, lung, rectal or melanoma tumor respectively," thus the specification teaches how to make and use the claimed subject matter (p. 18 of response).

Applicants' arguments have been fully considered but have not been found to be persuasive. Being overexpressed in normal stomach, lung, rectal or skin tissue compared to stomach, lung, rectal or melanoma tumor is not a functional limitation. Even if the specification provided support for diagnosing stomach, lung, rectal or melanoma tumors with PRO1335, the skilled artisan would not know how to use polypeptide sequences having sequences at least 80%, 85%, 90%, 95%, or 99% sequence identity to PRO1335 for diagnosing stomach, lung, rectal or melanoma tumors. Similarly, one skilled in the art would not know how to engineer a sequence such that it is overexpressed in certain tissues.

The rejection of claims 1-5 and 12-13 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement, is maintained for reasons of record on p. 6-7of paper no. 0704.

Applicants argue that the claims have been amended to provide that the claimed polypeptides are more highly expressed in normal stomach, lung, rectal or skin tissue compared to stomach, lung, rectal or melanoma tumors respectively. Thus, Applicants argue that based on

the detailed description of the cloning and expression of variants of PRO 1335 in the specification, the description of the gene amplification assay, the actual reduction to practice of sequences SEQ ID NOS: 73 and 74, and the functional recitation in the instant claims, one skilled in the art would know that Applicants possessed the subject matter of the pending claims (p. 19 of response).

Applicants' arguments have been fully considered but have not been found to be persuasive. As stated above, the claims have no functional limitations. In addition, the specification does not provide a utility or function for PRO1335. The claimed polypeptides may have functions and structures which differ greatly from that of PRO1335, therefore one of skill in the art would not be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Conclusion

NO CLAIMS ARE ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel K. Hunnicutt whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKH
12/23/04